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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/744,072	07/02/2001	Stephen W. Scherer	086671/0113	2291

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EXAMINER	
SWITZER, JULIET CAROLINE	
ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 10/22/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/744,072	SCHERER ET AL.	
	Examiner	Art Unit	
	Juliet C. Switzer	1634	

-- The MAILING DATE of this communication app ars on the cover sheet with th correspond nce address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 June 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,3,5,6 and 20-35* is/are pending in the application.

4a) Of the above claim(s) *23-35* is/are withdrawn from consideration.

5)☒ Claim(s) *2 and 3* is/are allowed.

6)☒ Claim(s) *5,6 and 20-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This action is written in response to applicant's correspondence submitted 6/24/03. Claims 2, 3, 5, 6, and 22 have been amended, claims 1, 4, and 7-19 have been canceled, and claims 23-35 have been added. Claims 2, 3, 5, 6, and 20-35 are pending. Applicant's amendments and arguments have been thoroughly reviewed, but are not persuasive for the reasons that follow. Any rejections not reiterated in this action have been withdrawn. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. **This action is FINAL.**

Election/Restrictions

2. Newly submitted claims 23-35 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons:

The newly added claims are each drawn to isolated nucleic acid molecules that are separate and distinct from those previously claimed, and from one another. In particular, each of the newly added claims 23-35 are drawn to a separate variant of instant SEQ ID NO: 1. The original prosecution included nucleic acids specifically drawn to SEQ ID NO: 1, as well as two additional variants of SEQ ID NO: 1, namely SEQ ID NO: 3 and SEQ ID NO: 5. The search and examination of the twelve newly recited variants would pose an undue burden on the examiner because the search for each of these variant genes would be separate, requiring separate considerations in view of the art and also the additional statutes. Each variant has separate and distinct diagnostic and prognostic implications.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 23-35 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Priority

3. Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged. However, the provisional application upon which priority is claimed fails to provide adequate support under 35 U.S.C. 112 for claims 2-3, 5, 6, 20, 21, or 22 of this application. Applicant claims priority to two provisional applications, 60/092,495, filed 7/20/98 and 60/130,269, filed 4/21/99. Neither of these provisional applications provide adequate support for claims 2-3, 5, 6, 20, 21, or 22.

These claims each recite instant SEQ ID NO: 1 which was not recited in either of the original priority documents. As each claim is afforded only a single priority date, these claims do not receive priority back to the '495 application.

Applicant is referred to MPEP 706.02, which states, "If the application is a continuation-in-part of an earlier U.S. application, any claims in the new application not supported by the specification and claims of the parent application have an effective filing date equal to the filing date of the new application. Any claims which are fully supported under 35 U.S.C. 112 by the earlier parent application have the effective filing date of that earlier parent application." In essence, one claim is entitled to one priority date. As outlined above, the instant claims are

directed to embodiments which are entitled to different dates. Thus, the claim has not been fully supported by the earliest date, therefore the later date is the effective filing date.

Thus, the filing date of claims 2-3, 5, 6, 20, 21, or 22 for examination herein is considered to be the international filing date, 20 July 1999.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 5, 6 and 20-22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 5 and 6 are directed to isolated nucleic acid molecules containing a sequence encoding a protein tyrosine phosphatase which is associated with Lafora's disease. Claim 5 includes nucleic acids that that **comprise** SEQ ID NO: 3, while claim 6 includes nucleic acids that **comprise** SEQ ID NO: 5. Claims 20-22 recite isolated nucleic acid molecules that have recited percent identities to SEQ ID NO: 1, SEQ ID NO: 2, or SEQ ID NO: 3 or that hybridize to SEQ ID NO: 1, SEQ ID NO: 2, or SEQ ID NO: 3 under recited hybridization and wash conditions. However, the instant specification only describes a single full length sequence encoding a protein tyrosine phosphatase which is associated with Lafora's disease, that is SEQ

ID NO: 1. The specification describes two additional nucleic acids that are associated with Lafora's disease, SEQ ID NO: 3 and SEQ ID NO: 5.

In making a determination of whether the application complies with the written description requirement of 35 U.S.C. 112, first paragraph, it is necessary to understand what Applicant has possession of and what Applicant is claiming. From the specification, it is clear that Applicant has possession of instant SEQ ID NO: 1 which is a full length cDNA encoding a protein that has the signature protein tyrosine phosphatase domain (see Denu et al. Cell, Vol. 87, pages 361-364 and instant Figure 4C). Applicant is also in possession of two alternate transcripts that comprise portions of SEQ ID NO: 1, namely SEQ ID NO: 3 and SEQ ID NO: 5. The specification teaches that these two transcripts are incomplete coding sequences, noted particularly because they do not have ATG start sites (see p. 25). Thus, it is not clear if these sequences actually encode active protein tyrosine phosphatases, even though they contain the "signature domain," it is not known from the teachings of the specification if the missing portions of encoded protein are essential for proper folding of the protein and thus tyrosine phosphatase activity. The specification teaches that there are mutations associated with Lafora's disease in each of SEQ ID NO: 1, SEQ ID NO: 3, and SEQ ID NO: 5 (see Figure 3, for example, where SEQ ID NO: 1 is the consensus sequence, SEQ ID NO: 3 is transcript A and SEQ ID NO: 5 is transcript B). The subject matter which is claimed is described above.

The specification does not provide any written description as to how instant SEQ ID NO: 1, SEQ ID NO: 2, or SEQ ID NO: 3 can be modified and still retain their association with Lafora's disease or their ability to encode a tyrosine phosphatase. The specification and prior art provide a "signature domain" for proteins that are tyrosine phosphatases, but neither provide any

guidance as to how instant SEQ ID NO: 1 can be modified but still retain its ability to encode a protein tyrosine phosphatase, furthermore, the claims do not even require that this signature domain remain in tact or be included in any of the claimed nucleic acids.

Claims 20-22, while providing for a structural definition of the claimed nucleic acids do not provide a proper structure to function relationship to defined the claimed genus. The claims also fail to recite other relevant identifying characteristics (physical and/or chemical and/or functional characteristics coupled with a known or disclosed correlation between function and structure) sufficient to describe the claimed invention in such full, clear, concise and exact terms that a skilled artisan would recognize applicant was in possession of the claimed invention.

With regard to the written description, all of these claims encompass nucleic acid sequences different from those disclosed in the specific SEQ ID No:s which, for claims 20-22 include modifications by permitted by the % identity language and hybridization language for which no written description is provided in the specification.

It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that

> "...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

In the instant application, only the nucleic acid sequence of the disclosed SEQ ID Nos are described. Also, in Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), it was concluded that:

> "...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

In the application at the time of filing, there is no record or description which would demonstrate conception or written description of nucleic acid encoding a protein tyrosine phosphatases that is associated with Lafora's disease which has nucleic acids modified by addition, insertion, deletion, substitution or inversion with respect to SEQ ID NO: 1 but retaining correlative function in the claimed product. Nor has the specification provided any no record or description which would demonstrate conception or written description of nucleic acids that are associated with Lafora's disease which has nucleic acids modified by addition, insertion, deletion, substitution or inversion with respect to SEQ ID NO: 1, SEQ ID NO: 2, or SEQ ID NO: 3 but retaining correlative function in the claimed product.

6. Claims 5, 6, and 20-22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid encoding a protein tyrosine phosphatase which is associated with Lafora's disease wherein the nucleic acid sequence comprises instant SEQ ID NO: 1, OR for nucleic acids associated with Lafora's disease wherein the nucleic acids consist of instant SEQ ID NO: 3 or instant SEQ ID NO: 5, does not reasonably provide enablement for additional nucleic acids that are associated with Lafora's disease. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 20-22 recite isolated nucleic acid molecules that have recited percent identities to SEQ ID NO: 1, SEQ ID NO: 2, or SEQ ID NO: 3 or that hybridize to SEQ ID NO: 1, SEQ ID NO: 2, or SEQ ID NO: 3 under recited hybridization and wash conditions.

The specification teaches a single full length sequence encoding a protein tyrosine phosphatase which is associated with Lafora's disease, that is SEQ ID NO: 1. The specification describes two additional nucleic acids that are associated with Lafora's disease, SEQ ID NO: 3 and SEQ ID NO: 5. The specification teaches that instant SEQ ID NO: 1 is a full length cDNA encoding a protein that has the signature protein tyrosine phosphatase domain (page 25 and Figure 4C). Applicant is also in possession of two alternate transcripts that comprise portions of SEQ ID NO: 1, namely SEQ ID NO: 3 and SEQ ID NO: 5. The specification teaches that these two transcripts are incomplete coding sequences, noted particularly because they do not have ATG start sites (see p. 25). Thus, it is not clear if these sequences actually encode active protein tyrosine phosphatases, even though they contain the "signature domain." It is not known from the teachings of the specification if the missing portions of encoded protein are necessary for proper folding of the protein and thus tyrosine phosphatase activity. The specification teaches that there are mutations associated with Lafora's disease in each of SEQ ID NO: 1, SEQ ID NO: 3, and SEQ ID NO: 5 (see Figure 3, for example, where SEQ ID NO: 1 is the consensus sequence, SEQ ID NO: 3 is transcript A and SEQ ID NO: 5 is transcript B).

The specification does not provide any guidance as to how instant SEQ ID NO: 1, SEQ ID NO: 2, or SEQ ID NO: 3 can be modified and still retain their association with Lafora's disease and/or their ability to encode a tyrosine phosphatase. Furthermore, the specification does not demonstrate or confirm that SEQ ID NO: 2 and SEQ ID NO: 3 in fact encode protein tyrosine phosphatases, as even the specification itself teaches that these are not full length coding sequences. The specification and prior art provide a "signature domain" for proteins that are tyrosine phosphatases (see Denu et al. Cell, Vol. 87, pages 361-364), but neither provide any

guidance as to how instant SEQ ID NO: 1 can be modified but still retain its ability to encode a protein tyrosine phosphatase, furthermore, the claims do not even require that this signature domain remain in tact or be included in any of the claimed nucleic acids.

The identification of additional nucleic acids of fragments of the instantly disclosed nucleic acids which retain association with Lafora's disease and/or encode polypeptides that retain tyrosine phosphatase activity is highly unpredictable. The activity of a protein is dependent on the folding of the polypeptide chain, and the location of the active site relative to the rest of the protein (see for example, Denu et al. who describe the structure of protein tyrosine phosphatases). Small changes in the amino acid sequence of a polypeptide can disrupt this folding and thus the ability of a polypeptide to function. Additionally, it is highly unpredictable what sequences of nucleic acid will be associated with a particular disease. In order to identify additional sequences, the ordinary practitioner would be required to undertake analysis of many, many patients to screen for additional sequences whose presence is an indicator of disease.

In light of the lack of guidance in the specification and prior art, the lack of additional working examples, the high level of unpredictability in the field of the invention and the high quantity of experimentation necessary to practice the claimed invention, it is concluded that undue experimentation would be required to practice the claimed invention commensurate in scope with the instant claims.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claim 22 is rejected under 35 U.S.C. 102(b) as being anticipated by Bartnik et al. (EP 0705842).

Bartnik et al. teach an isolated nucleic acid that would hybridize to a nucleic acid sequence set forth in SEQ ID NO: 1, SEQ ID NO: 3, or SEQ ID NO: 5 under the stringency conditions recited in the claims. The nucleic acid TAU10(1) taught by Bartnik et al. has 98.9% similarity with instant SEQ ID NO: 1 over nucleotides 2669-2849 of instant SEQ ID NO: 1.

```
Qy   2669 GGAGATGACATTTGCTTTGGGCAGAGGCAGCTAGCCAGGACACATTTCCACTATAATTTT 2728
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1 GGAGATGACATTTGCTTTGGGCAGAGGCAGCTAGCCAGGACACATTTCCACTATAATTTT 60

Qy   2729 ACAAAGTTAAATTTATAAGCTAGCATTAAGTAAAGTGAAG-TCCAGCTCCCTTGCTAAAA 2787
           ||||||||||||||||||||||||||||||||||||||| ||||||||||||||||||||
Db     61 ACAAAGTTAAATTTATAAGCTAGCATTAAGTAAAGTGAAGTTCCAGCTCCCTTGCTAAAA 120

Qy   2788 ATAACTAGAGGTAATAATTGGTATTCAGGTAACTCATTTACAGTCATAATGTGTTGTGAA 2847
           ||||||||||||||||||||||||||||||||||||||| |||||||||||||||||||
Db    121 ATAACTAGAGGTAATAATTGGTATTCAGGTAACTCATTTACA-TCATAATGTGTTGTGAA 179

Qy   2848 AA 2849
           ||
Db    180 AA 181
```

In the alignment, the top sequence is a portion of instant SEQ ID NO: 1, and the bottom sequence is TAU10(1). The TAU10(1) sequence has 98.9% local similarity over nucleotides 2481-2661 of instant SEQ ID NO: 3, and 96.4% local similarity over nucleotides 466-631 of instant SEQ ID NO: 5. Such a nucleic acid would hybridize to any one of SEQ ID NO: 1, SEQ ID NO: 3, or SEQ ID NO: 5 under the recited conditions. With regard to the newly added functional limitations of the claim, the nucleic acid taught by Bartnik *et al.* appears to be

substantially identical to the claimed nucleic acid, as it meets all of the structural requirements of the claims. Thus, this rejection is maintained even though Bartnik *et al.* do not recited the functional limitations of claim 22. Applicant is reminded that MPEP 2112.01 teaches "Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). 'When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not.'"

9. Claims 20, 21, and 22 are rejected under 35 U.S.C. 102(a) as being anticipated by Serratosa et al. (Human Molecular Genetics, Feb. 1999, Vol. 8, No. 2).

This reference is a 102(a) reference against these claims because the claims were not granted priority back to the provisional applications. Thus, the filing date of these claims is the instant filing date, 20 July 1999.

Serratosa et al. provide an isolated nucleic acid that is associated with Lafora's disease and encodes a putative protein tyrosine phosphatase (p. 346 and Fig. 4). Serratosa et al. teach an isolated nucleic acid that has 88.5% identity with instant SEQ ID NO: 1. The nucleic acid taught by Serratosa et al. is described as a "composite sequence" of a number of cDNA transcripts, and was deposited in GenBank under accession AJ130763 (Fig. 2). For Applicant's convenience, the GenBank record is provided. Nucleotides 1-2805 of nucleic acid taught by Serratosa et al. share 99.8% identity with SEQ ID NO: 1 over nucleotides 242-2805 of instant SEQ ID NO: 1.

```
Query Match             88.5%;  Score 2767.2;  DB 9;  Length 2805;
Best Local Similarity   99.8%;  Pred. No. 0;
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  Matches 2802;  Conservative    0;  Mismatches    3;  Indels    3;  Gaps    3;

Qy    242 TGGACACGTTCTGGTACAAGTTCCTGAAGCGGGAGCCGGGAGGAGAGCTCTCCCTGGGAAG 301
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1 TGGACACGTTCTGGTACAAGTTCCTGAAGCGGGAGCCGGGAGGAGAGCTCTCCCTGGGAAG 60

Qy    302 GCAATGGACCTCATCATGACCGTTGCTGTACTTACAATGAAAACAACTTGGTGGATGGTG 361
          |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     61 GCAATGGACCTCATCATGACCGTTGCTGTACTTACAATGAAAACAACTTGGTGGATGGTG 120

Qy    362 TGTATTGTCTCCCAATAGGACACTGGATTGAGGCCACTGGGCACACCAATGAAATGAAGC 421
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    121 TGTATTGTCTCCCAATAGGACACTGGATTGAGGCCACTGGGCACACCAATGAAATGAAGC 180

Qy    422 ACACAACAGACTTCTATTTTAATATTGCAGGCCACCAAGCCATGCATTATTCAAGAATTC 481
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    181 ACACAACAGACTTCTATTTTAATATTGCAGGCCACCAAGCCATGCATTATTCAAGAATTC 240

Qy    482 TACCAAATATCTGGCTGGGTAGCTGCCCTCGTCAGGTGGAACATGTTACCATCAAACTGA 541
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    241 TACCAAATATCTGGCTGGGTAGCTGCCCTCGTCAGGTGGAACATGTTACCATCAAACTGA 300

Qy    542 AGCATGAATTGGGGATTACAGCTGTAATGAATTTCCAGACTGAATGGGATATTGTACAGA 601
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    301 AGCATGAATTGGGGATTACAGCTGTAATGAATTTCCAGACTGAATGGGATATTGTACAGA 360

Qy    602 ATTCCTCAGGCTGTAACCGCTACCCAGAGCCCATGACTCCAGACACTATGATTAAACTAT 661
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    361 ATTCCTCAGGCTGTAACCGCTACCCAGAGCCCATGACTCCAGACACTATGATTAAACTAT 420

Qy    662 ATAGGGAAGAAGGCTTGGCCTACATCTGGATGCCAACACCAGATATGAGCACCGAAGGCC 721
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    421 ATAGGGAAGAAGGCTTGGCCTACATCTGGATGCCAACACCAGATATGAGCACCGAAGGCC 480

Qy    722 GAGTACAGATGCTGCCCCAGGCGGTGTGCCTGCTGCATGCGCTGCTGGAGAAGGGACACA 781
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    481 GAGTACAGATGCTGCCCCAGGCGGTGTGCCTGCTGCATGCGCTGCTGGAGAAGGGACACA 540

Qy    782 TCGTGTACGTGCACTGCAACGCTGGGGTGGGCCGCTCCACCGCGGCTGTCTGCGGCTGGC 841
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    541 TCGTGTACGTGCACTGCAACGCTGGGGTGGGCCGCTCCACCGCGGCTGTCTGCGGCTGGC 600

Qy    842 TCCAGTATGTGATGGGCTGGAATCTGAGGAAGGTGCAGTATTTCCTCATGGCCAAGAGGC 901
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    601 TCCAGTATGTGATGGGCTGGAATCTGAGGAAGGTGCAGTATTTCCTCATGGCCAAGAGGC 660

Qy    902 CGGCTGTCTACATTGACGAAGAGGCCTTGGCCCGGGCACAAGAAGATTTTTTCCAGAAAT 961
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    661 CGGCTGTCTACATTGACGAAGAGGCCTTGGCCCGGGCACAAGAAGATTTTTTCCAGAAAT 720

Qy    962 TTGGGAAGGTTCGTTCTTCTGTGTGTAGCCTGTAGCTGGTCAGCCTGCTTCTGCCCCCTC 1021
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    721 TTGGGAAGGTTCGTTCTTCTGTGTGTAGCCTGTAGCTGGTCAGCCTGCTTCTGCCCCCTC 780

Qy   1022 CTGATTTCCCTAAGGAGCCTGGGATGATGTTGGTCAAATGACCTAGAAACAAGGATTCTA 1081
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    781 CTGATTTCCCTAAGGAGCCTGGGATGATGTTGGTCAAATGACCTAGAAACAAGGATTCTA 840

Qy   1082 CCTGAACTGAAAGGACTGTGTGACCTCCCCAAGCCAACCACTTTCACCTGGGATGACTTT 1141
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    841 CCTGAACTGAAAGGACTGTGTGACCTCCCCAAGCCAACCACTTTCACCTGGGATGACTTT 900

Qy   1142 CGATTATGCTTTGGTTTGGGGCTGTATTTTTGAAATACTCTACAAGAAAGCTGTGGCTCA 1201
          ||||||||||| ||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    901 CGATTATGCTTTGTTTTGGGGCTGTATTTTTGAAATACTCTACAAGAAAGCTGTGGCTCA 960

Qy   1202 ACACATGAGAAGAAGCACGAAGCAGTTAGGCTGTACATCAGACAGAAGGGTAATGCGTGC 1261
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Db      961 ACACATGAGAAGAAGCACGAAGCAGTTAGGCTGTACATCAGACAGAAGGGTAATGCGTGC 1020

Qy     1262 AGTTCCTGCTGCCTGCAGGCAGACGAGGCCTTTGCTTTACAGCACTGTATGTGTTGCACG 1321

Db     1021 AGTTCCTGCTGCCTGCAGGCAGACGAGGCCTTTGCTTTACAGCACTGTATGTGTTGCACG 1080

Qy     1322 ATGGATCCGTGACAGCACTTTCCTGTTGCACTGAAACTCTTGGCCATGTAGAGGAAAAGA 1381

Db     1081 ATGGATCCGTGACAGCACTTTCCTGTTGCACTGAAACTCTTGGCCATGTAGAGGAAAAGA 1140

Qy     1382 TATGGAGTTATGTGGATTTCATCACTAGTATGTGTGCCGTGAGCTGGTCAGTTGCCAAAG 1441

Db     1141 TATGGAGTTATGTGGATTTCATCACTAGTATGTGTG-CGTGAGCTGGTCAGTTGCCAAAG 1199

Qy     1442 GAGGAAATAAGGTTAGAAGCCTGAACCGTTACAAAAGAAGAGCTCACTATGGTCAAAAAG 1501

Db     1200 GAGGAAATAAGGTTAGAAGCCTGAACCGTTACAAAAGAAGAGCTCACTATGGTCAAAAAG 1259

Qy     1502 TGATGGCTTTCAGGACTTGTTTTTTATCCTGCCTCACAGTTGTTAAAGTCTGTTCCAAGG 1561

Db     1260 TGATGGCTTTCAGGACTTGTTTTTTATCCTGCCTCACAGTTGTTAAAGTCTGTTCCAAGG 1319

Qy     1562 CATCACCTTCCTTCTCTACCCAACAACCCTGTGTAACAACTAAAGTAGAATTATCTCTCA 1621

Db     1320 CATCACCTTCCTTCTCTACCCAACAACCCTGTGTAACAACTAAAGTAGAATTATCTCTCA 1379

Qy     1622 TTTGTTGGTGGTTTTTCCTCAAAATTACCAAACAAAGCAAAAAATACCCTTGTTTTTTAT 1681

Db     1380 TTTGTT-GTTGTTTTTCCTCAAAATTACCAAACAAAGCAAAAAATACCCTTGTTTTTTAT 1438

Qy     1682 AGTTGAGATGTCAAGGAAGTTAAATTGAGGCTTAATGAGCATAGGTAGCTTGTCCAAGGT 1741

Db     1439 AGTTGAGATGTCAA-GAAGTTAAATTGAGGCTTAATGAGCATAGGTAGCTTGTCCAAGGT 1497

Qy     1742 CTCATGACCAGTCAAGGGCAAGCTGGAGTTAATAATCTATATTTATTTGACTCAGCACTG 1801

Db     1498 CTCATGACCAGTCAAGGGCAAGCTGGAGTTAATAATCTATATTTATTTGACTCAGCACTG 1557

Qy     1802 TTTTCATCACAACTTGTTTTCCCAGCATCATGTAGTGCATTTAGTTTGTCTTTCTCAGG 1861

Db     1558 TTTTCATCACAACTTGTTTTCCCAGCATCATGTAGTGCATTTAGTTTGTCTTTCTCAGG 1617

Qy     1862 GTATAGTCAATATGCCTGCAGGAGTTTCTATAGCGAGACATAGAATAGTATTCTGATCAG 1921

Db     1618 GTATAGTCAATATGCCTGCAGGAGTTTCTATAGCGAGACATAGAATAGTATTCTGATCAG 1677

Qy     1922 TTGCCAAAGAATCTAGGAAATTAGTTGTATTTTGTGCAAGCTAATTTAAAAACATGATGG 1981

Db     1678 TTGCCAAAGAATCTAGGAAATTAGTTGTATTTTGTGCAAGCTAATTTAAAAACATGATGG 1737

Qy     1982 GCTGTTTTAAGACCAGAGTGGAAATTCATGAGAGGAACTATACTACCAAAAGAGCCCAAA 2041

Db     1738 GCTGTTTTAAGACCAGAGTGGAAATTCATGAGAGGAACTATACTACCAAAAGAGCCCAAA 1797

Qy     2042 TGACCAAATCCATGGATAATTGCTTCACAGCCTTGGCCATCCTGGCTCAGCTCTCAATTT 2101

Db     1798 TGACCAAATCCATGGATAATTGCTTCACAGCCTTGGCCATCCTGGCTCAGCTCTCAATTT 1857

Qy     2102 AGTATAATATGCAGTTCCTGTGCCTCCAGACTATGCAGCTCATCACCCTAGGTTCTACAG 2161

Db     1858 AGTATAATATGCAGTTCCTGTGCCTCCAGACTATGCAGCTCATCACCCTAGGTTCTACAG 1917

Qy     2162 GAAATACAGAGATGAACAACTTTGCCTTCAAAAAATGTGCTGCCTAGAAAACAGACCTGC 2221

Db     1918 GAAATACAGAGATGAACAACTTTGCCTTCAAAAAATGTGCTGCCTAGAAAACAGACCTGC 1977
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Qy    2222 ATTTCAACCCAACTGTAATGCAGGATTTGGACCATGAATGATATGCTAGAATAGAAGAAA 2281
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1978 ATTTCAACCCAACTGTAATGCAGGATTTGGACCATGAATGATATGCTAGAATAGAAGAAA 2037

Qy    2282 GAGAAGTGTTTTTTTTAATTGAGAGCCTCTATGTGCAAGGTGATATATAATCATATCCAGT 2341
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    2038 GAGAAGTGTTTTTTTTAATTGAGAGCCTCTATGTGCAAGGTGATATATAATCATATCCAGT 2097

Qy    2342 TTAATCTTCACAATATCCAATGAAGAAGGTCTCATTATCTCCATGATAAAGATGGGGAAA 2401
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    2098 TTAATCTTCACAATATCCAATGAAGAAGGTCTCATTATCTCCATGATAAAGATGGGGAAA 2157

Qy    2402 CTAAGGTCAGAAGGGTTAACTCAACTGTCTATTGTCACATGATGAATAAATAGATGAAGT 2461
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    2158 CTAAGGTCAGAAGGGTTAACTCAACTGTCTATTGTCACATGATGAATAAATAGATGAAGT 2217

Qy    2462 GAGATACAAAGCTGGGTTTGATTCAAAGCCCTTACTTTCCTAATTAAACTATGATGCGTA 2521
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    2218 GAGATACAAAGCTGGGTTTGATTCAAAGCCCTTACTTTCCTAATTAAACTATGATGCGTA 2277

Qy    2522 TTTATTTTTCTGCACCTTCCTTTCTTCCACAAACACATATTGATAGATGCAAGAGACTCT 2581
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    2278 TTTATTTTTCTGCACCTTCCTTTCTTCCACAAACACATATTGATAGATGCAAGAGACTCT 2337

Qy    2582 TATTTATAAGGCGTGGGGGACAAGAAGGATACAAGGTAAGTTTCAGTGGAGCTCAGAGGA 2641
           |||||| ||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    2338 TATTTAGAAGGCGTGGGGGACAAGAAGGATACAAGGTAAGTTTCAGTGGAGCTCAGAGGA 2397

Qy    2642 CGGGGAGATAGAACTGTGGCACTTAGGGGAGATGACATTTGCTTTGGGCAGAGGCAGCTA 2701
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    2398 CGGGGAGATAGAACTGTGGCACTTAGGGGAGATGACATTTGCTTTGGGCAGAGGCAGCTA 2457

Qy    2702 GCCAGGACACATTTCCACTATAATTTTACAAAGTTAAATTTATAAGCTAGCATTAAGTAA 2761
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    2458 GCCAGGACACATTTCCACTATAATTTTACAAAGTTAAATTTATAAGCTAGCATTAAGTAA 2517

Qy    2762 AGTGAAGTCCAGCTCCCTTGCTAAAAATAACTAGAGGTAATAATTGGTATTCAGGTAACT 2821
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    2518 AGTGAAGTCCAGCTCCCTTGCTAAAAATAACTAGAGGTAATAATTGGTATTCAGGTAACT 2577

Qy    2822 CATTTACAGTCATAATGTGTTGTGAAAATTTAATCTTAAAAATTAAATTTTTAAACTATG 2881
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    2578 CATTTACAGTCATAATGTGTTGTGAAAATTTAATCTTAAAAATTAAATTTTTAAACTATG 2637

Qy    2882 TGGGTCTGTGAATTTCTTTAATGTCTAAGAAATCCAGCTTCATAATTTCCATGATACAAA 2941
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    2638 TGGGTCTGTGAATTTCTTTAATGTCTAAGAAATCCAGCTTCATAATTTCCATGATACAAA 2697

Qy    2942 GATCTTTTTTCAGGTGGATTTTTACCTTTGTTCCTTTTGCTCTGATAGACAAAATCAGTT 3001
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    2698 GATCTTTTTTCAGGTGGATTTTTACCTTTGTTCCTTTTGCTCTGATAGACAAAATCAGTT 2757

Qy    3002 TAGGACTATTAAAGAATGTTTTGGAATAAACTGTCTTTTCCTCAATG 3049
           |||||||||||||||||||||||||||||||||||||||||||||||
Db    2758 TAGGACTATTAAAGAATGTTTTGGAATAAACTGTCTTTTCCTCAATG 2805
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In the alignment, the nucleic acid marked "Qy" is instant SEQ ID NO: 1, and the nucleic acid marked "Db" is the nucleic acid provided by Serratosa et al. The same nucleic acid shares 93.7% identity with instant SEQ ID NO: 3, and 99.5% local similarity over nucleotides 54-2861

of instant SEQ ID NO: 3. With regard to SEQ ID NO: 5, the nucleic acid taught by Serratosa et al. has 98.5% local identity with SEQ ID NO: 5, when nucleotides 224-685 of the nucleic acid taught by Serratosa et al. are aligned with nucleotides 17-478 of instant SEQ ID NO: 5.

It is noted that Serratosa et al. postulate that this nucleic acid encodes a putative protein tyrosine phosphatase, but do not demonstrate the activity of such a protein. The examiner is unable to undertake such an analysis, as a laboratory is not available. The rejection is applied in the interest of compact prosecution since the teachings of the Serratosa et al. reference meet all of the structural limitations provided in the claims.

10. Claims 5, 6, 20, 21, and 22 are rejected under 35 U.S.C. 102(a) as being anticipated by Minassian et al. (Nature Genetics, Volume 20, pages 171-174, October 1998).

It is noted that the authorship of the Minassian et al. reference is distinct from the inventorship of the instant application and that this rejection may be overcome by the filing of a 132 Katz-type declaration.

This reference is a 102(a) reference against these claims because the claims were not granted priority back to the provisional applications. Thus, the filing date of these claims is the instant filing date, 20 July 1999.

Minassian et al. provide an isolated nucleic acid that is associated with Lafora's disease and encodes a putative protein tyrosine phosphatase (p. 172, Fig. 4c). Minassian et al. a nucleic acid sequence identical to the nucleotide sequence in instant figure 4A, see their Figure 4A. Additionally, teach an isolated nucleic acid comprising transcript B, which is identical to the isolated nucleic acid whose sequence is given in instant figure 9 (see their Figure 3 and Figure 4 and the figure legend of Fig. 4).

The nucleotide sequence provided by Minassian et al. would hybridize under conditions of high stringency with instant SEQ ID NO: 1, and comprise at least 15 bases of instant SEQ ID NO: 1. No alignment of instant SEQ ID NO: 1 to the sequence provided in Minassian et al. is available, but at least nucleotides 189-597 of instant SEQ ID NO: 1 are identical to nucleotides 1-408 of the sequence taught in Figure 4A of the disclosure of Minassian.

It is noted that Minassian et al. postulate that this nucleic acid encodes a putative protein tyrosine phosphatase, but do not demonstrate the activity of such a protein. The examiner is unable to undertake such an analysis, as a laboratory is not available. The rejection is applied in the interest of compact prosecution since the teachings of the Minassian et al. reference meet all of the structural limitations provided in the claims.

Response to Remarks

Priority

As noted in the "Priority" section, it is agreed by both the examiner and applicant that nucleic acids consisting of instant SEQ ID NO: 3 and SEQ ID NO: 5 are disclosed in the '495 provisional. However, instant claims 5 and 6 are not so limited, as they encompass nucleic acids "comprising" SEQ ID NO: 3 and SEQ ID NO: 5, and subsequently are not supported by 112 1st paragraph in the instant application or in the provisional application (see Written Description and Enablement rejections). Essentially these claims do not have support in the specification due to the fact that they are drawn using open claim language, and because they recite that the transcripts encode protein tyrosine phosphatases, as discussed in the rejections. Claims which are limited to nucleic acids consisting of instant SEQ ID NO: 3 or SEQ ID NO: 5 would be entitled to the earliest priority date and would thus be free of the prior art. Furthermore, it is

noted that claims 20-22 each continue to recite instant SEQ ID NO: 1 and are therefore entitled to only the instant filing date, as each claim is granted only a single filing date.

Claim Objections and 112 2nd paragraph rejections

These are withdrawn in light of applicant's amendments to the claims.

112 1st paragraph

Applicant's argue that claims 20-22 are supported in the disclosure as there is clear support for the claim language on page 5, lines 10-23 of the application as filed. However, the verbatim support referred to by applicants does not address the question of written description from the standpoint of possession of the molecules claimed or in fact sufficient description of them. Applicant's argument does not address the issues raised in the rejection, for example with regard to the size of the claimed genus versus the showing in the specification, or the open claim language versus the fact that it is not clear that applicant is in possession of full length coding sequences that comprise instant SEQ ID NO: 3 or instant SEQ ID NO: 5. Thus, the rejection is maintained.

With regard to the rejection for scope of enablement, applicants merely state that they are entitled to homologous sequences or those that hybridize as recited in claims 20-22, but applicants do not provide any arguments or evidence in support of this statement. For the reasons in the rejection, the rejection is maintained.

102 rejections

With regard to the newly added functional limitations of the claim, the nucleic acid taught by Bartnik *et al.* appears to be substantially identical to the claimed nucleic acid, as it meets all of the structural requirements of the claims. Thus, this rejection is maintained even

though Bartnik *et al.* do not recited the functional limitations of claim 22. Applicant is reminded that MPEP 2112.01 teaches "Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). 'When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not.'"

Applicants arguments with regard to the 102(a) rejections reiterate their claim to priority. For reasons already discussed (see "Priority" headings herein), this is not persuasive and the rejections are maintained.

Conclusion

11. Claims 2 and 3 are allowed.

12. Claims drawn to isolated nucleic acids that are associated with Lafora's disease wherein the nucleic acids **consist** of instant SEQ ID NO: 3 or instant SEQ ID NO: 5 would meet the written description and enablement requirements, because these sequences have mutations in them that are associated with Lafora's disease, and thus one would know how to make and use them to detect Lafora's disease.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C. Switzer whose telephone number is 703 306 5824. The examiner can normally be reached on Monday through Friday, from 9:00 AM until 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on 703 308 1152. The fax phone numbers for the organization where this application or proceeding is assigned are 703 305 3592 and (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 308 0196.

Juliet C. Switzer
Patent Examiner
Art Unit 1634

October 19, 2003

GARY BENZION, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600